Abdominal Imaging

Published online: 30 June 2015

Abdom Imaging (2015) 40:3240–3247
DOI: 10.1007/s00261-015-0496-7

Percutaneous recanalization for combined-type Budd–Chiari syndrome: strategy and long-term outcome

Yu-Fei Fu,[1] Yu Li,[1] Yan-Feng Cui,[2] Ning Wei,[2] De-Chun Li,[1] Hao Xu[2]

[1]Department of Radiology, Xuzhou Central Hospital, 199 South Jie-fang Road, Xuzhou 221009, China
[2]Department of Interventional Radiology, The Affiliated Hospital of Xuzhou Medical College, 99 West Huai-hai Road, Xuzhou 221006, China

Abstract

Purpose: To investigate the feasibility, strategy, and long-term outcome of percutaneous recanalization for combined-type Budd–Chiari syndrome (BCS).
Methods: From December 2007 to August 2014, consecutive symptomatic combined-type BCS patients were treated by percutaneous recanalization in our centers. Inferior vena cava (IVC) recanalization was the first-stage treatment for all patients. Recanalization of one hepatic vein (HV) was the second-stage treatment for the selected patients. If the patient had the compensatory and patent accessory HV (AHV), we observed this patient for 7 days after IVC recanalization. If the symptoms of portal hypertension improved, HV recanalization was not needed. Otherwise, HV recanalization was performed. If the patient had no patent AHV, HV recanalization was performed 3 days after IVC recanalization. Data on technical success, clinical success, and follow-up were analyzed, respectively.
Results: Sixty-two symptomatic combined-type BCS patients were enrolled. Technical success of percutaneous recanalization was achieved in 60 patients. Among them, 52 patients had the patent AHV and underwent single IVC recanalization, and 8 patients had no patent AHV and underwent combined IVC and HV recanalization. Clinical success was achieved in all of the 60 patients. Three patients died during the follow-up. The cumulative 1-, 2-, and 4-year survival rates were 98.3%, 96.5%, and 92.7%, respectively.
Conclusion: Percutaneous recanalization is suitable for most combined-type BCS patients. Treatment strategy can be made according to the situation of AHV. If the patient has the patent AHV, single IVC recanalization is enough. Otherwise, combined IVC and HV recanalization should be performed.

Key words: Budd–Chiari syndrome—Recanalization—Inferior vena cava—Hepatic vein

Budd–Chiari syndrome (BCS) is a rare disease characterized by hepatic venous outflow obstruction [1–8]. According to the different locations of the obstructed site, BCS can be divided into three types: (a) inferior vena cava (IVC)-type BCS is defined as IVC obstruction with at least one patent hepatic vein (HV); (b) HV-type BCS is defined as obstruction of the three main HVs; and (c) combined-type BCS is defined as obstruction of both IVC and three main HVs [1]. At present, IVC-type BCS patients are usually treated by IVC recanalization [2–4]. The strategy of treatment of HV-type BCS patients is relatively complex. Medical treatment can hardly improve patients' symptoms [5]. HV recanalization can be suitable for most HV-type BCS patients [6, 7]. If the HV recanalization still fails, transjugular intrahepatic portosystemic shunt (TIPS) should be considered [5, 8]. However, there is less study of treatment strategy about combined BCS. In this study, we reported our clinical results of percutaneous recanalization for combined-type BCS.

Methods

This study was approved by our Institutional Review Board. Each patient received details of percutaneous recanalization and provided written informed consent for percutaneous recanalization before treatment.

Yu-Fei Fu and Yu Li have contributed equally to this work.

Correspondence to: Hao Xu; *email:* xuhao587@163.com

Patient selection

From December 2007 to August 2014, consecutive symptomatic combined-type BCS patients were treated by percutaneous recanalization in our centers. Patients were excluded if they had BCS secondary to malignant tumor, had asymptomatic BCS due to well-established intra- and extra-hepatic collateral vessels, or underwent TIPS, surgical shunt, or liver transplant. Patients' baseline data before treatment included age, sex, symptoms, imaging findings, and laboratory examination findings.

Diagnosis

Diagnosis of combined-type BCS was established by reviewing patients' history, abdominal ultrasound findings, and abdominal magnetic resonance angiography (MRA, Fig. 1)/computed tomography angiography (CTA) findings. The length of the obstruction of IVC and three HVs was measured by MRA/CTA. The membranous obstruction of IVC/HV is defined as an obstruction length ≤1 cm, and segmental obstruction of IVC/HV is defined as an obstruction length >1 cm [9]. All patients were investigated for confirming whether they had the compensatory and patent accessory HV (AHV) by ultrasound and MRA/CTA before treatment. The diameter of AHV stem was measured from the results of MRA/CTA. A compensatory AHV is defined as an AHV with its stem ≥5 mm [10]. All patients' blood samples were collected for checking the risk factors of BCS (JAK2 mutation, Protein C deficiency, Protein S deficiency, and Factor V Leiden mutation) before treatment. Symptomatic BCS is defined as a BCS with any one of the following clinical manifestations: abdominal pain, abdominal distention, jaundice, ascites, variceal bleeding, encephalopathy, or lower extremity edema [1].

Fig. 2. **A–C** Single IVC recanalization for the combined-type BCS patient with patent AHV. **A** IVC venography confirmed the IVC obstruction and two patent AHVs (*arrow*). **B**, **C** IVC was patent after balloon dilation. The obstructed HV was not treated. ►

Treatment procedure

All procedures were performed by three interventional radiologists. Blood pressure, heart rate, arterial oxygen

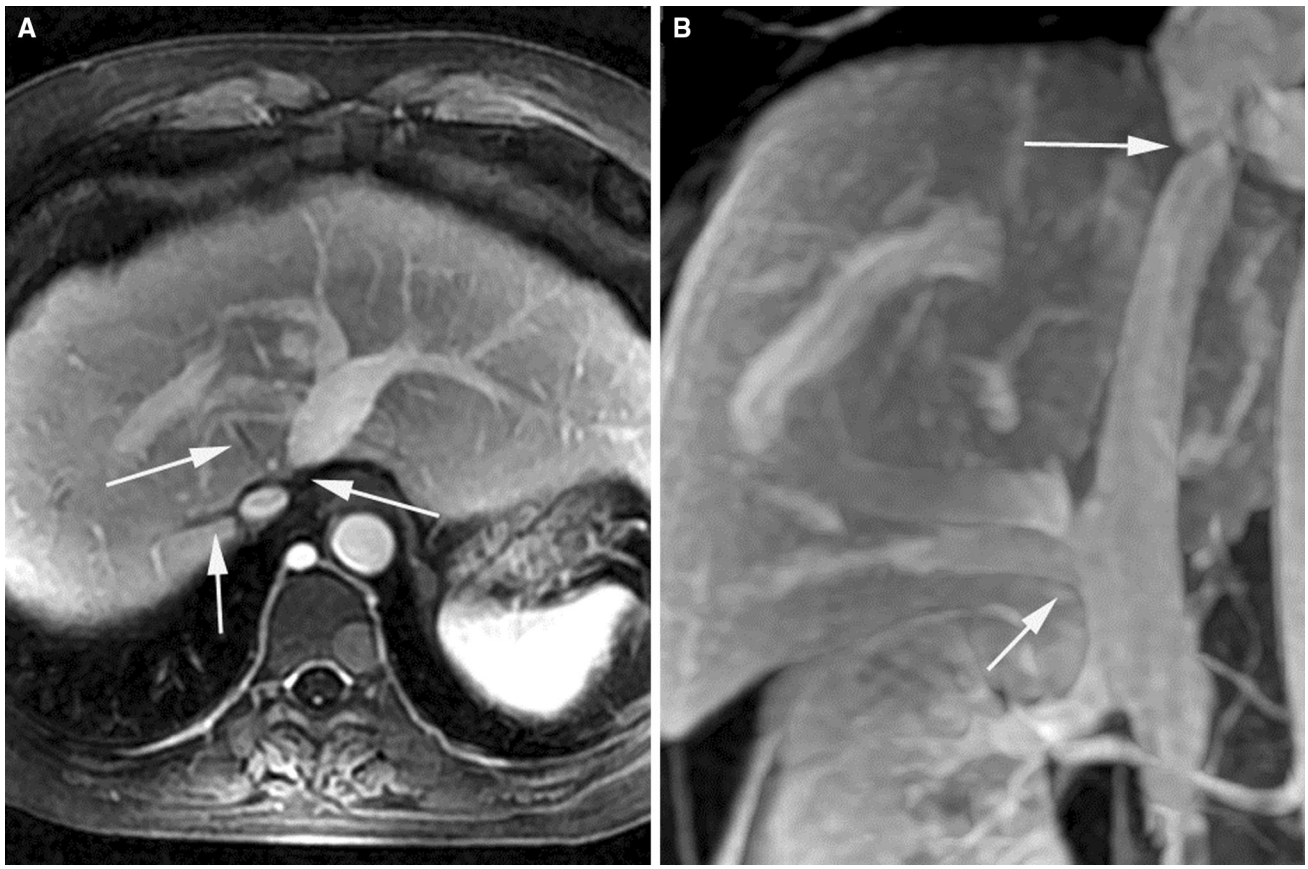
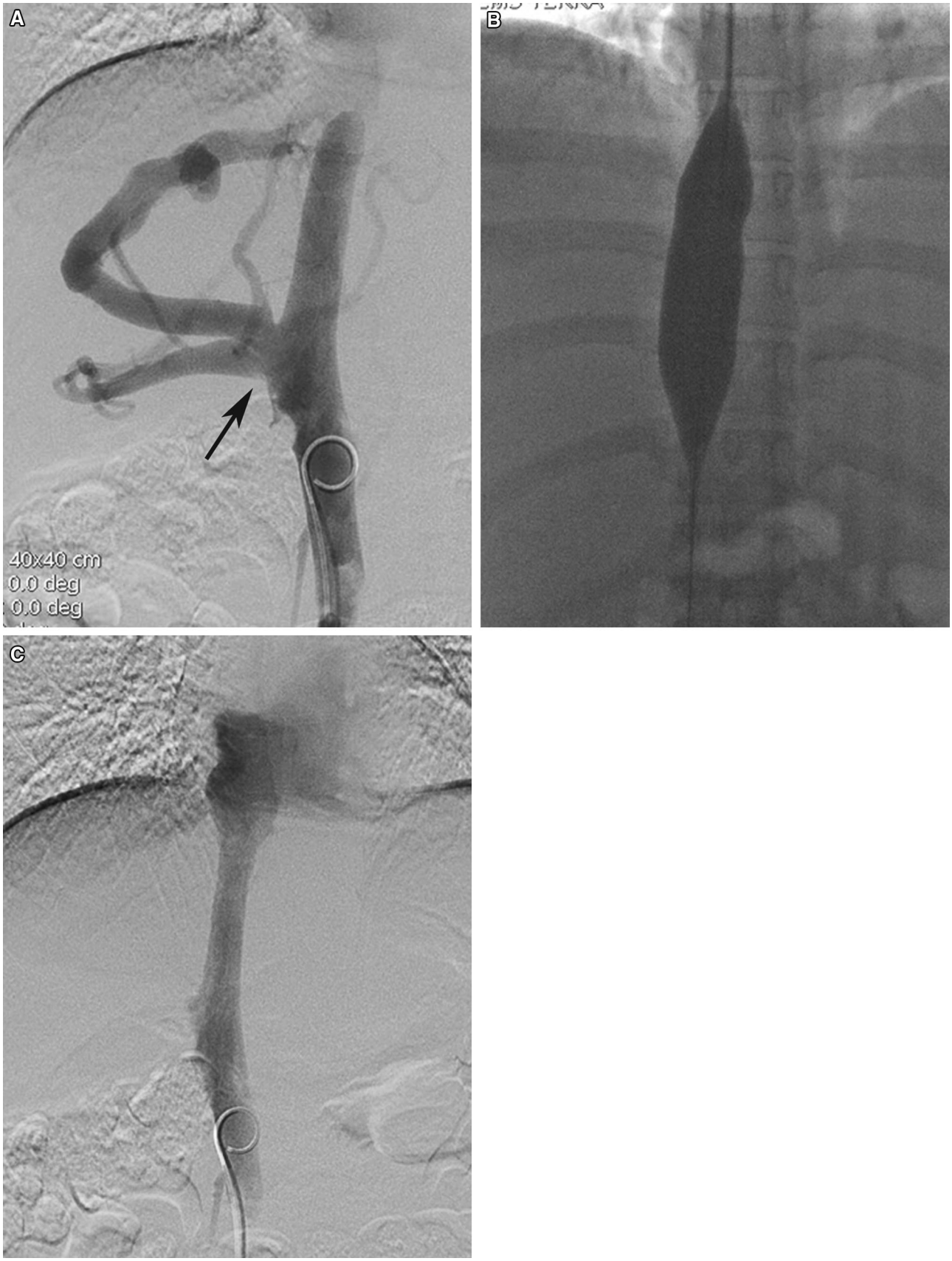


Fig. 1. **A**, **B** Diagnosis of combined-type BCS on MRA. **A** Axial abdominal MRA demonstrated the obstruction of three main HVs (*arrows*). **B** The coronal MRA demonstrated the IVC obstruction (*long arrow*) and the compensatory and two patent AHVs (*short arrow*).


A
40x40 cm
0.0 deg
0.0 deg
B
C

saturation, and respiration rate were monitored throughout the treatment.

First-stage treatment—IVC recanalization was the first-stage treatment for all patients. A 5F Pigtail catheter (Cordis, Warren, New Jersey, USA) was inserted into the distal IVC obstruction from the right femoral vein, and the IVC venography was performed. Then, a 4F VER catheter (Cordis) and a 0.035-inch guide wire (Terumo, Tokyo, Japan) were used to access the IVC obstruction. If this was achieved, IVC recanalization was performed via the transfemoral approach. If the guide wire could not pass through the IVC obstruction, a J-type steel needle (Cook, Bloomington, Ind. USA) was used to puncture the IVC obstruction from the top to the bottom end via transjugular approach. When this was achieved, the IVC recanalization was performed via the combined transjugular and transfemoral approaches.

Second-stage treatment—recanalization of one HV was the second-stage treatment for the selected patients. (a) If the patient had the patent and compensatory AHV, we observed this patient for 7 days after IVC recanalization. If the symptoms of portal hypertension improved, HV recanalization was not needed (Fig. 2). Otherwise, HV recanalization was performed. (b) If the patient had no patent AHV, HV recanalization was performed 3 days after IVC recanalization. The one HV with the shortest obstruction length was chosen as the target HV. HV recanalization was routinely performed via the transjugular approach. If the transjugular HV recanalization failed, the ultrasound-guided percutaneous transhepatic route would be used to access the HV and the HV recanalization would be performed via the combined transhepatic and transjugular approaches.

Percutaneous recanalization was performed with the balloon or stent. Stent insertion was performed if there was more than 30% residual stenosis after balloon dilation [1]. IVC and HV pressure were measured by a piezometer tube before and after recanalization. After treatment, all patients received subcutaneous low-molecular-wight heparin (5000 IU, twice a day) for 3 days, followed by oral warfarin for 12 months. The dose of warfarin was adjusted to maintain the international normal ratio of 2:3.

Assessment

Technical success of percutaneous recanalization was defined as the hepatic outflow obstruction restored at venography with disappearance of intra- and extra-hepatic collateral vessels. Clinical success was defined as the symptoms and liver function tests improved after technical success of percutaneous recanalization [1].

All patients underwent abdominal ultrasound and clinical examination 7 days, 1, 3, 6, and then every 6 months after treatment to confirm the long-term effectiveness. Re-obstruction was defined as no or retrograde flow present in lumen or if the degree of lumen obstruction was more than 30% with intrahepatic collateral vessels on ultrasound examination [1]. Re-obstruction was suspected if the BCS-related symptoms reappeared. Follow-up ended at the patients' death, the point of undergoing TIPS, surgical shunt, or liver transplant, the point of lost in the follow-up, or the point of setting this study (February 2015).

Statistical analysis

Continuous variables are summarized as mean ± standard deviation or median. The paired-samples t test or Wilcoxon test was performed to compare variables before and after treatment. Categorical variables were compared by x^2 test or Fisher exact test. Cumulative recanalization patency was calculated using Kaplan–Meier curves. A p value <0.05 was considered statistically significant. All statistical calculations were performed using SPSS 16.0 (Chicago, IL, USA).

Table 1. Baseline data of the 60 patients with technical success

	Values
Total number	60
Age (years)	47.3 ± 11.5 (24–72)
Male/Female	33/27
Duration of symptoms (months)	14.4 ± 7.8 (2–35)
Risk factors	
JAK2 mutation	0
Protein C deficiency	0
Protein S deficiency	0
Factor V Leiden mutation	0
Imaging finding	
IVC obstruction (MO/SO)	43/17
Right HV obstruction (MO/SO)	22/38
Middle HV obstruction (MO/SO)	20/40
Left HV obstruction (MO/SO)	23/37
Patients with patent AHV	52
Combined IVC thrombosis	10
Laboratory tests	
Prothrombin time (PT, s)	14.7 ± 2.3 (11.6–25.9)
International normalized ratio (INR)	1.2 ± 0.2 (0.86–1.95)
Aspartate aminotransferase (AST, U/L)	28.6 ± 21. 4 (9–125)
Alanine aminotransaminase (ALT, U/L)	31.7 ± 12.2 (16–81)
Alkaline phosphatase (ALP, U/L)	124.9 ± 56.9 (43–312)
Total bilirubin (TBIL, μmol/L)	36.6 ± 18.1 (12.7–107.8)
Albumin (g/L)	38.6 ± 5.6 (26.4–48.4)
Creatinine (μmol/L)	58.4 ± 17.0 (34–122)
Alpha fetoprotein (AFP, μg/L)	7.6 ± 10.3 (0.7–48.4)
Carcinoembryonic antigen (CEA, ng/mL)	2.4 ± 1.6 (0.2–11.7)
Cancer antigen 125 (CA125, U/mL)	96.6 ± 108.5 (7.5–475.7)
Cancer antigen 19-9 (CA19-9, U/mL)	12.5 ± 8.2 (0.1–39.7)
Child-Pugh score	7.3 ± 1.5 (5–11)
BCS-TIPS score	10.3 ± 3.3 (6.3–24.1)
Rotterdam score	1.0 ± 0.4 (0.1–1.5)
New Clichy score	4.6 ± 1.4 (2.4–9.3)

IVC Inferior vena cava, *HV* hepatic vein, *AHV* accessory hepatic vein, *MO* membranous obstruction, *SO* segmental obstruction

Results

Patients

During the enrolled period, a total of 62 symptomatic combined-type BCS patients were enrolled in this study. Two patients had hepatic cellular carcinoma (HCC). The diagnosis of HCC was confirmed by ultrasound- or CT-guided transhepatic aspiration biopsy. But the HCC was not the cause of BCS, and thus these 2 patients were not excluded.

Technical success

Technical success of percutaneous recanalization was achieved in 60 (96.8%) patients. The baseline data of these 60 patients are demonstrated in Table 1. The remaining 2 patients successfully underwent IVC recanalization, but they failed to undergo HV recanalization because of the total obstruction of all three main HVs. These 2 patients underwent TIPS ($n = 1$) or medical treatment only ($n = 1$). Among the 60 patients, 10 patients had IVC thrombosis and underwent catheter-directed thrombolysis (urokinase, 300,000 IU each day) for 2–7 days (mean 4.8 ± 1.7 days) before IVC recanalization. The thrombi were completely dissolved in these 10 patients. Three patients experienced right groin hematoma after treatment, and they were successfully managed by local pressure.

Table 2 demonstrated the details of treatment procedures. The IVC balloons were 26–30 mm in diameter and 40–50 mm in length (Optimed, Ettlingen, Germany or Cook). The HV balloons were 10–14 mm in diameter and 40 mm in length (Cook). The IVC stents were Z-type bare stents with a diameter of 28–30 mm and a length of 70–90 mm (Yongtong, Shenyang, China). The HV stents were Zilver stents with a diameter of 10–14 mm and a length of 40 mm (Cook). The mean IVC pressure decreased from 30.8 ± 3.9 cm H_2O before treatment to 12.8 ± 4.1 cm H_2O after treatment (paired-samples t test, $p = 0.000$, 1 cm H_2O = 0.098 kPa). The median HV pressure decreased from 44.5 cm H_2O before treatment to 21.5 cm H_2O after treatment (Wilcoxon test, $p = 0.012$).

Clinical success

Clinical success of single IVC recanalization was achieved in all patients with patent AHV. A total of 65 AHVs were found in these 52 patients with patent AHV. The mean diameter of the 65 AHVs was 8.1 ± 2.8 mm (range 5–21 mm). Clinical success of combined IVC and HV recanalization was achieved in all patients without patent AHV. Table 3 demonstrates the improvements of symptoms after treatment.

Liver function improvements

We compared aspartate aminotransferase (AST, normal range: 0–40 U/L), alanine aminotransaminase (ALT, normal range: 0–40 U/L), albumin (normal range 35–55 g/L), and total bilirubin (TBIL, normal range: 1.7–20 μmol/L) before and after treatment to evaluate the improvement of liver function. AST, ALT, albumin, and TBIL values were abnormal in 11, 15, 13, and 52 patients before treatment, respectively. The number of patients with abnormal liver function indices decreased progressively after treatment (Table 4). The mean abnormal preoperative AST, ALT, albumin, and TBIL values improved from 60.3 ± 32.7, 50.3 ± 10.7 U/L, 30.5 ± 2.5 g/L, and 39.8 ± 17.4 μmol/L to 41.9 ± 14.3 U/L (paired-samples t test, $p = 0.011$), 42.3 ± 7.3 U/L (paired-samples t test, $p = 0.000$), 33.7 ± 2.7 g/L (paired-samples t test, $p = 0.000$), and 29.4 ± 14.2 μmol/L (paired-samples t test, $p = 0.000$) 1 month after treatment, respectively. The normal preoperative AST, ALT, albumin, and TBIL were still normal at 1 month after treatment. The abnormal 1-month postoperative AST value improved from 41–76 to 36–43 U/L 3 months after treatment. The median

Table 2. Details of treatment procedure

	Patients with patent AHV ($n = 52$)	Patients without patent AHV ($n = 8$)
Single IVC recanalization		
IVC balloon dilation	45	0
IVC stent	7	0
Combined IVC and HV recanalization		
IVC balloon dilation + HV balloon dilation	0	6
IVC stent + HV balloon dilation	0	0
IVC balloon dilation + HV stent	0	1
IVC stent + HV stent	0	1
IVC recanalization approach		
Transfemoral	24	3
Combined transjugular and transfemoral	28	5
HV recanalization approach		
Transjugular	0	7
Combined transhepatic and transjugular	0	1

IVC inferior vena cava, *HV* hepatic vein, *AHV* accessory HV

Table 3. Improvements in symptoms after treatment

	Before treatment (No.)	1 Month after treatment (No.)		3 Months after treatment (No.)	
		Disappearance	Improved	Disappearance	Improved
Abdominal distension	52	41	11	52	0
Abdominal pain	48	43	5	48	0
Ascites	45	33	12	40	5
Hepatomegaly	42	28	14	36	6
Splenomegaly	38	20	18	32	6
Gastrointestinal bleeding	7	7	0	7	0
Chest–abdominal varix	49	40	9	47	2
Lower extremity edema	46	40	6	45	1

Table 4. Number of patients with normal and abnormal liver function indices before and after treatment

	Before treatment (No.)		1 Month after treatment (No.)		3 Months after treatment (No.)	
	Normal	Abnormal	Normal	Abnormal	Normal	Abnormal
AST	49	11	56	4	58	2
ALT	45	15	53	7	59	1
Total bilirubin	8	52	20	40	43	17
Albumin	47	13	52	8	58	2

AST aspartate aminotransferase, *ALT* alanine aminotransaminase

abnormal 1-month postoperative ALT and albumin values improved from 41 U/L and 32.9 g/L to 36 U/L (Wilcoxon test, $p = 0.018$) and 35.8 g/L (Wilcoxon test, $p = 0.012$) 3 months after treatment, respectively. The mean abnormal 1-month postoperative TBIL value improved from 32.9 ± 14.5 to 21.4 ± 7.4 μmol/L (paired-samples t test, $p = 0.000$) 3 months after treatment. The normal 1-month postoperative AST, ALT, albumin, and TBIL were still normal at 3 months after treatment.

Patency

During a follow-up of 6–74 months (mean 34.8 ± 9.9 months), no patient was lost in the follow-up, 11 patients (six patients with patent AHV and 5 patients without patent AHV) experienced re-obstruction of IVC ($n = 10$) or HV ($n = 1$). There was no significant difference between re-obstruction of IVC and HV (10/60 vs. 1/8, $p = 0.764$). The cumulative 1-, 2-, and 4-year primary patency rates were 88.2%, 84.6%, and 78.6%, respectively. These patients were successfully revised by repeat IVC balloon dilation ($n = 9$), IVC stent insertion ($n = 1$), or HV balloon dilation ($n = 1$). The cumulative 1-, 2-, and 4-year secondary patency rates were 98.3%, 94.6%, and 86.0%, respectively (Fig. 3).

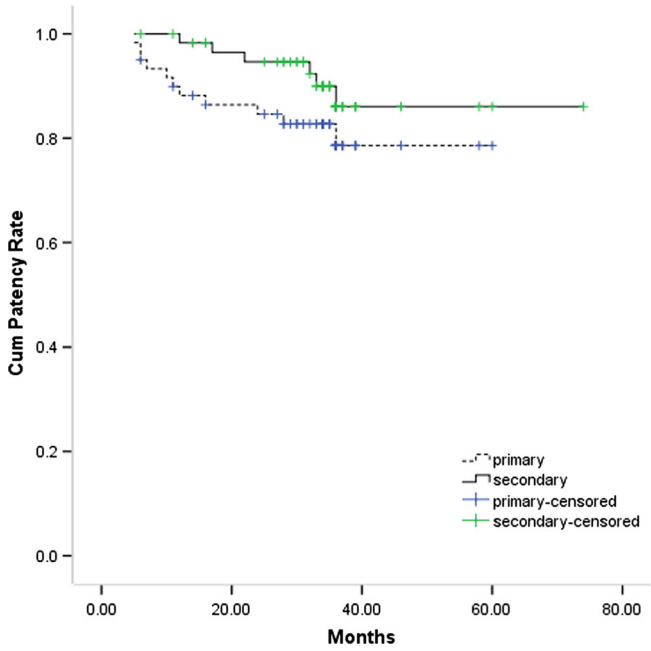


Fig. 3. The primary and secondary patency rates after treatment.

Survival

Three patients (two patients with patent AHV and 1 patient without patent AHV) died at 11–36 months (median 24 months) after treatment. There was no significant difference of death between patients with and without patent AHV (2/52 vs. 1/8, $p = 0.296$). The causes of death were HCC ($n = 2$) or recurrence of gastrointestinal bleeding ($n = 1$). The cumulative 1-, 2-, and 4-year survival rates were 98.3%, 96.5%, and 92.7%, respectively (Fig. 4).

Discussion

This study demonstrated the feasibility, strategy, and long-term results of percutaneous recanalization for combined-type BCS. Initial results were positive. Percutaneous recanalization was suitable for 60 of 62 (96.8%)

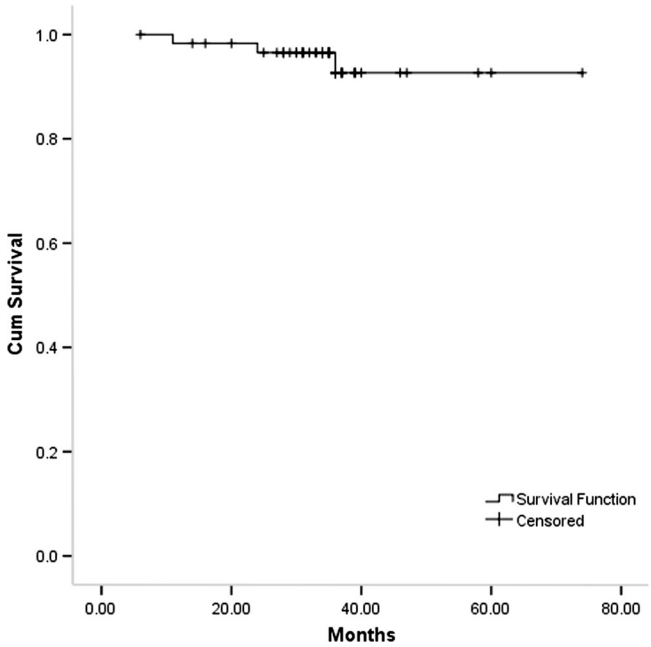


Fig. 4. The survival rates after treatment.

patients. Clinical success was achieved in all of the 60 patients with technical success. Long-term results were also favorable.

Approximately 14.7%–24.0% BCS cases are combined-type BCS [9, 11]. Combined IVC recanalization and HV recanalization or TIPS is considered as the reasonable treatment strategy for combined-type BCS [9, 11]. The purpose of combined IVC and HV recanalization is to establish a hepatic drainage way from HV to right atrium. Zhang et al. [9] have reported their successful experience of combined IVC and HV recanalization for 17 combined-type BCS patients.

In this study, the treatment strategy for combined-type BCS patients was not all the same as that for combined-type BCS patients in the previous studies [9, 11]. Patent AHV was an important factor in making the treatment strategy. There were 52 of 60 patients (86.7%) having the patent AHV in this study. Our results demonstrated that single IVC recanalization could achieve the clinical success in all of these 52 patients. AHV is an intrahepatic vein which connects to the IVC and constitutes the hepatic drainage vein [10, 12, 13]. AHV is usually thin in the healthy people [13], but it usually becomes dilated in the BCS patients because the increased hepatic pressure can cause the hepatic blood to flow into the AHV via the intrahepatic collateral vessels [10, 12, 13]. If the ostium of AHV is patent, the hepatic blood can flow from liver to IVC via the AHV, and thus the HV recanalization can be avoided.

For the remaining 8 patients without patent AHV, combined IVC and HV recanalization was performed. Recanalization of one HV can afford to drain the entire liver because of the well-established intrahepatic collateral vessels between the HVs [9].

The long-term patency and survival rates in this study may indicate that percutaneous recanalization can provide a favorable outcome for combined-type BCS patients. The high secondary patency rates also demonstrated that percutaneous recanalization is well repeatable.

This study has some limitations. First, the biggest limitation is its retrospective nature. Further randomized controlled trials should be performed. Second, there is no control group in this study. However, our purpose was investigating the feasibility, strategy, and long-term results of percutaneous recanalization for combined-type BCS. Third, the sample size is small due to the rarity of this type of BCS.

In conclusion, although further clinical trials are needed, our results may indicate that percutaneous recanalization is suitable for most combined-type BCS patients. Treatment strategy can be made according to the situation of AHV. If the patient has the patent AHV, single IVC recanalization is enough. Otherwise, combined IVC and HV recanalization should be performed.

Compliance with Ethical Standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. For this type of study formal consent is not required.This article does not contain any studies with animals performed by any of the authors.

Informed consent Informed consent was obtained from all individual participants included in the study.

References

1. Han G, Qi X, Zhang W, et al. (2013) Percutaneous recanalization for Budd-Chiari syndrome: an 11-year retrospective study on patency and survival in 177 Chinese patients from a single center. Radiology 266:657–667
2. Ding PX, Li YD, Han XW, et al. (2011) Treatment of Budd-Chiari syndrome with urokinase following predilation in patients with old inferior vena cava thrombosis. Radiol Med 116:56–60
3. Zhang Q, Huang Q, Shen B, et al. (2014) Efficacy and safety of endovascular intervention for the management of primary entire-inferior vena cava Occlusion. Cardiovasc Interv Radiol. doi: 10.1007/s00270-014-0980-4
4. Zhang QQ, Xu H, Zu MH, et al. (2014) Strategy and long-term outcomes of endovascular treatment for Budd-Chiari syndrome complicated by inferior vena caval thrombosis. Eur J Vasc Endovasc Surg 47:550–557
5. Fitsiori K, Tsitskari M, Kelekis A, et al. (2014) Transjugular intrahepatic portosystemic shunt for the treatment of Budd-Chiari syndrome patients: results from a single center. Cardiovasc Interv Radiol 37:691–697
6. Zhang Q, Xu H, Zu M, et al. (2013) Catheter–directed thrombolytic therapy combined with angioplasty for hepatic vein obstruction in Budd-Chiari syndrome complicated by thrombosis. Exp Ther Med 6:1015–1021

7. Sang HF, Li XQ (2014) Endovascular treatment of Budd-Chiari syndrome with hepatic vein obstruction in China. J Laparoendosc Adv Surg Tech A 24:846–851
8. Eapen CE, Velissaris D, Heydtmann M, et al. (2006) Favourable medium term outcome following hepatic vein recanalisation and/or transjugular intrahepatic portosystemic shunt for Budd Chiari syndrome. Gut 55:878–884
9. Zhang CQ, Fu LN, Xu L, et al. (2003) Long-term effect of stent placement in 115 patients with Budd-Chiari syndrome. World J Gastroenterol 9:2587–2591
10. Fu YF, Wei N, Wu Q, et al. (2015) Use of accessory hepatic vein intervention in the treatment of Budd-Chiari syndrome. Cardiovasc Interv Radiol. doi:10.1007/s00270-015-1105-4
11. Kathuria R, Srivastava A, Yachha SK, et al. (2014) Budd-Chiari syndrome in children: clinical features, percutaneous radiological intervention, and outcome. Eur J Gastroenterol Hepatol 26:1030–1038
12. Fu YF, Xu H, Zhang K, et al. (2015) Accessory hepatic vein recanalization for treatment of Budd-Chiari syndrome due to long-segment obstruction of the hepatic vein: initial clinical experience. Diagn Interv Radiol 21:148–153
13. Tang W, Zhang XM, Yang L, et al. (2011) Hepatic caudate vein in Budd-Chiari syndrome: depiction by using magnetic resonance imaging. Eur J Radiol 77:143–148